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Ziv Dadon, MD, Nir Levi, MD, Amir Orlev, MD, Daniel Belman, MD, Evan Avraham Alpert, MD, Michael Glikson, MD, Shmuel Gottlieb, MD, Adi Butnaru, MD

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The Utility of Hand-held Cardiac and Lung Ultrasound in Predicting Outcomes of Hospitalized Patients with COVID-19

Ziv Dadon MD,^{*a} Nir Levi MD,^{*a} Amir Orlev MD,^a Daniel Belman MD,^b Evan Avraham Alpert MD,^{c,d} Michael Glikson MD,^{a,d} Shmuel Gottlieb MD,^{**a,e}
Adi Butnaru MD^{**a}

^aJesselson Integrated Heart Center, ^bIntensive Care Unit, and ^cEmergency Department, Shaare Zedek Medical Center, ^dFaculty of Medicine Hebrew University, Jerusalem, ^eSackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

* Drs. Dadon and Levi contributed equally.

**Drs. Gottlieb and Butnaru contributed equally.

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Address for correspondence:

Shmuel Gottlieb, MD

Jesselson Integrated Heart Center, Shaare Zedek Medical Center

Shmu'el-Bait St 12

Jerusalem, 9103102, Israel, Tel: +972-26555975

E-mail: shmuelg@ekmd.huji.ac.il

Brief summary

We characterized the utility of hand-held echocardiogram in COVID-19 hospitalized patients in predicting endpoints based on identified cardiac abnormalities (ventricular/valvular pathologies). An abnormal echocardiogram is associated with a higher burden of comorbidities and independently predicts major outcomes. The utilization of a hand-held echocardiogram is an important “rule-out” tool among COVID-19 high-risk patients and should be integrated into their routine admission evaluation.

Abstract

Background: Strict isolation precautions limit formal echocardiogram use in the setting of COVID-19 infection. Information on the importance of the utilization of a hand-held focused ultrasound for cardiac evaluation in these patients is scarce. This study investigated the utility of a hand-held echocardiogram device in COVID-19 hospitalized patients in diagnosing cardiac pathologies and predicting the composite endpoint of in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure.

Methods: From April 28th through July 27th, 2020, consecutive patients diagnosed with COVID-19 underwent evaluation using a hand-held ultrasound (Vscan Extend™ with Dual Probe; GE Healthcare) within 48-h of admission. The patients were divided into two groups: 'Normal' and 'Abnormal' (as defined by biventricular systolic dysfunction/enlargement, or moderate/severe valvular regurgitation/stenosis) echocardiogram study.

Results: Among 102 patients, 26 (25.5%) had an abnormal study. They were older, with more co-morbidities, and more severe presenting symptoms, as compared to the group with a normal echocardiogram. The prevalence of the composite outcome among low- and high-risk patients (oxygen saturation <94%) was 3.1% and 27.1%, respectively. Multivariate logistic regression analysis revealed that an abnormal echocardiogram at presentation was independently associated with the composite endpoint (OR 6.19; 95% CI 1.50-25.57, p=0.012).

Conclusions: An abnormal echocardiogram in COVID-19 infection settings is associated with a higher burden of medical comorbidities and independently predict major adverse endpoints. Hand-held focused echocardiogram can be utilized as an important “rule-out” tool among high-risk COVID-19 patients and should be integrated

into their routine admission evaluation. However, its routine utilization among low-risk patients is not recommended.

Keywords: Abnormal cardiac systolic function; COVID-19; Hand-held echocardiogram; Prognosis; Risk stratification.

Introduction

COVID-19 interacts with the cardiovascular system on multiple levels. It is well established that known cardiovascular disease or risk factors are associated with a significant increase in morbidity and mortality among COVID-19 patients. In addition, it has been demonstrated that elevation in cardiac biomarkers such as high-sensitivity cardiac troponin-I (hs-cTnI) is correlated with a poor prognosis in COVID-19 patients.[1]

The association between COVID-19 and the cardiovascular system has led researchers to try to better identify predictors for severe disease and adverse outcomes. Possible predictors for disease severity might be cardiac systolic function, including left and right ventricular (RV) systolic function or valvular functional abnormalities as determined by echocardiogram. Routine echocardiographic evaluation of all patients admitted with COVID 19, however, is currently discouraged according to various guidelines and consensus papers due to concerns of excessive workload in the setting of a pandemic,[2,3] risk of infection of echocardiogram professionals, and equipment contamination which increases with long imaging time.[4]

Hand-held ultrasound has been shown to be accurate when used by cardiologists for many aspects of cardiac evaluation. This includes evaluation of left ventricular ejection fraction (LVEF), regional wall motion abnormalities, left ventricular (LV) hypertrophy, inferior vena cava size, valvular pathology and pericardial effusion.[5,6] As the use of point-of-care ultrasound (POCUS) is increasingly being employed, its application in cardiac systolic function assessment is likely to markedly increase.[7,8] LVEF, RV systolic function, as well as basic valvular function can be determined upon admission by bedside echocardiogram using the POCUS approach.[9,10] In addition, echocardiogram using hand-held devices can be operated by non-cardiologists, does

not need a sonography technician, can be easily cleaned and can be stored in COVID-19 units for ease of use without disruption to the clinical setting. Furthermore, some devices can be utilized for lung assessment as well with a quick and > 90% accurate interpretation for common causes of acute respiratory failure.[11]

The objective of this study is to characterize the utility of hand-held echocardiogram in COVID-19 hospitalized patients to predict endpoints based on identified cardiac abnormalities including ventricular size and systolic function, and valvular pathologies.

Methods

Study setting

This is a prospective study of real-time focused echocardiogram and lung ultrasound performed using a hand-held device. The study was conducted on consecutive PCR-confirmed COVID-19 patients hospitalized in designated medical wards at a tertiary care medical center from April 28th through July 27th, 2020. The study was approved by the hospital's Institutional Review Board.

All echocardiographic clips were acquired by cardiologists or intensivists and were later interpreted by a fellowship-trained echocardiographer. Variables including demographics, past medical history, electrocardiogram (ECG), imaging modalities, and laboratory results were obtained from the medical record.

Study endpoints

The primary endpoint was defined as a composite endpoint of in-hospital death, mechanical ventilation, shock and acute decompensated heart failure (ADHF). Secondary endpoints included the composite endpoint, individual parameters of the composite endpoint, advanced ventilatory support (high-flow nasal cannula, non-invasive positive airway pressure support and invasive ventilation), chronic ventilation,

myocardial injury (defined as >3 times hs-cTnI upper normal limit), venous thromboembolism, anti-COVID-19 drug use, sepsis and length of hospital stay.

Study protocol

Confirmed COVID-19 patients who were hospitalized in designated internal medicine departments were recruited into the study. Conscious patients consented verbally. Patients who were not able to give informed consent underwent echocardiogram if it was clinically indicated. Patients that refused to participate in the study were excluded. Basic characteristics included age, sex and known previous medical illness. A routine chest X-ray, ECG, and blood workup were performed for every patient upon admission to the designated COVID-19 wards. The routine laboratory tests included complete blood count, renal function, electrolytes, hs-cTnI, D-dimer, coagulation function tests and C-reactive protein (CRP). Brain natriuretic peptide (BNP) was measured based on the clinical judgment of the treating physician. The study physicians performing the ultrasound examination wore personal protective equipment including a full gown, N95 face mask, face shield, and at least two sets of gloves. Participants were evaluated by focused echocardiogram examination and lung ultrasound within 48 hours of their hospitalization using a hand-held ultrasound machine (Vscan Extend™ with Dual Probe; General Electric, Northville, MI). The cardiac POCUS was conducted using the sector transducer from the apical, parasternal and substernal views. Valves were evaluated visually using both 2D and color Doppler echocardiogram. The acquired video clips were stored in the Digital Imaging and Communications in Medicine (DICOM) format and sent wirelessly to a picture archiving and utilization platform (McKesson Cardiology™, version 14.0 TX, USA) routinely used by the Cardiology Department. The echocardiogram clips were then interpreted using visual evaluation by an experienced echocardiographer (AB), blinded to the patient's clinical

course and presentation, for evaluation of LVEF and LV diameter, RV visual systolic function and diameter, severity of valvular dysfunction (the valve were visually assessed for functional abnormalities, i.e. regurgitation or stenosis, using both the 2D and Doppler echocardiogram), pericardial effusion and any additional significant echocardiographic findings. Offline measurements of LV end-diastolic diameter (LVEDD), tricuspid annular plane systolic excursion (TAPSE) and fractional area change (FAC) were completed. POCUS lung ultrasound was completed using the linear transducer and included a 10-location assessment (standard approach- 4 quadrants on each anterior hemithorax and 2 on each posterior hemithorax) for B-lines, subpleural consolidations/lung hepatization and pleural effusions. Each assessed variable was graded separately for each location according to the severity from 0 (normal), though 1 (several lines or small consolidation/effusion) to 2 (coalescent B-lines or diffuse/widespread consolidation/effusion). The lung ultrasound assessment scoring was calculated as the sum of the entire graded variables (range of 0-20).

Data management

All data obtained in this study were entered into two Microsoft Excel spreadsheets. One file contained the case identifying number, patient identifiers and other pertinent variables. POCUS results were inserted into a second file using the patient's identifying number. The two files were then matched.

Study participants were divided into normal or abnormal echocardiograms according to POCUS results. Abnormal echocardiograms included those with LVEF <50%, LV dilation, RV systolic dysfunction/dilation, or moderate/severe valvular dysfunction (functional regurgitation or stenosis).

Statistical Analyses

The patients were divided into normal and abnormal echocardiograms, and analyses were performed accordingly. Descriptive statistics were used to analyze differences in baseline and clinical characteristics, echocardiogram and lung ultrasound results and endpoints, using Chi-square or Fisher's exact tests for categorical variables, and the t-test or Mann-Whitney U test for continuous variables, where appropriate. Test selection was based on data distribution and normalcy.

High-risk patients were defined as those with room-air saturation of $< 94\%$. The ability of the echocardiogram results to identify patients with and without the composite outcome was then tested for sensitivity, specificity, positive predictive value and negative predictive value among low and high-risk patients.

Odds ratio (OR) and 95% confidence interval (CI) were calculated to test the univariate associations between abnormal echocardiogram and composite endpoint and individual endpoints.

Multivariate logistic regression analysis (OR and 95% CI) was calculated for the association between abnormal echocardiogram and the composite endpoint among the entire cohort and individually among high-risk patients, including pertinent baseline characteristics covariates (those with p values of less than 0.05). Statistical analyses were performed using SPSS Statistics for Windows version 21 (SPSS Inc., Chicago, IL).

Results

A total of 102 COVID-19 hospitalized patients were recruited into the study, including 76 (74.5%) with a normal and 26 (25.5%) with an abnormal echocardiogram (Table 1). Four patients refused to participate in the trial and thus were excluded.

Baseline and medical characteristics

As shown in Table 1, the mean age of the total cohort was 59.7 ± 18.4 years, 63.7% were males. Patients with an abnormal echocardiogram were older and more likely to suffer from comorbidities including smoking, hypertension, hyperlipidemia, ischemic heart disease, past revascularization, and heart failure (HF), as compared to patients with a normal echocardiogram. They had a higher proportion of past valve replacement and cardiac implantable electronic devices. Moreover, they were treated more often with chronic HF evidence-based medications, anti-platelets, diuretics, and statins.

Presentation characteristics and laboratory results

As shown in Table 1, the two groups did not differ in terms of their presenting complaints nor vital signs. Patients with an abnormal echocardiogram had a higher rate of pathological electrocardiograms (including non-specific and ST-segment changes or T-wave inversion) and chest x-ray infiltrates, as compared to those with a normal echocardiogram. Laboratory results of creatinine, hs-cTnI, fibrinogen, activated-partial thromboplastin time, white blood cell count, neutrophil/lymphocyte count ratio, CRP and D-dimer were higher in the abnormal as compared to the normal echocardiogram group while albumin was lower.

Echocardiogram and lung ultrasound results

Echocardiogram and lung ultrasound results are presented in Table 2. As compared to patients with a normal echocardiogram, those with an abnormal study had a lower LVEF ($49.2 \pm 8.2\%$ vs. $57.2 \pm 4.1\%$, $p < 0.001$), higher LVEDD (4.8 ± 0.6 vs. 4.5 ± 0.5 , $p = 0.016$), and a higher proportion of LVEF $< 50\%$, RV systolic dysfunction and dilation, pericardial effusion, and significant valvulopathy (including significant mitral and tricuspid regurgitation, and aortic stenosis). Comparing lung scores between patients with a normal echocardiogram, to those with abnormal echocardiograms yielded no association (2.9 ± 2.4 vs. 3.7 ± 2.5 , $p = 0.119$).

Four patients underwent an official echocardiogram following the study exam during the index hospitalization, which confirmed the findings of the focused echocardiogram.

Results among patients with and without advanced ventilatory support

Echocardiogram results and measurements among patients with and without advanced ventilatory support are also presented in Table 2. As compared with patients with no advanced ventilatory support, patients with such support had a higher proportion of ventricular abnormalities (38.5% vs. 18.4%, $p=0.034$), a lower TAPSE (1.8 ± 0.2 vs. 2.0 ± 0.3 cm, $p=0.045$) and a higher lung score (4.5 ± 2.4 vs. 2.7 ± 2.3 , $p=0.001$). The groups did not differ in other assessed or measured POCUS parameters.

Sensitivity and specificity among low- and high-risk patients

Among the 102 patients included in the study, only 32 are defined as low-risk patients (with room air oxygen saturation $\geq 94\%$) including 6 patients with an abnormal echocardiogram from which only 1 patient had the composite outcome. The sensitivity of focused echocardiogram for the composite outcome among low-risk patients is 100% and the specificity is 83.9% with a PPV of 16.7% and NPV of 100%.

Among the 70 patients defined as high-risk (with room air oxygen saturation $< 94\%$), the sensitivity of focused exam for the composite outcome is 57.9% and the specificity is 82.4% with a PPV of 55.0% and NPV of 84.0%.

Association between abnormal echocardiogram and study endpoints

The associations between an abnormal echocardiogram and the endpoints are presented in Table 3 and Figure 1. An abnormal echocardiogram was associated with the endpoints of the need for advanced ventilatory support, ADHF, myocardial injury, acute kidney injury, death, and with the composite endpoint (in-hospital death, mechanical ventilation, shock, and ADHF; unadjusted OR 7.29, 95% CI 2.44-20.00).

Multivariate analysis adjusting for age, heart failure, ischemic heart disease, smoking, hypertension, hyperlipidemia, prior revascularization, cardiovascular implantable electronic device (CIED) implantation or valve replacement revealed that among the entire cohort an abnormal echocardiogram was independently associated with a higher probability for the composite endpoint (OR 6.19; 95% CI 1.50-25.57, $p=0.012$).

Multivariate analysis adjusting for age, heart failure, hypertension, hyperlipidemia, smoking and CIED implantation revealed that among high-risk patients an abnormal echocardiogram was independently associated with a higher probability for the composite endpoint (OR 5.47; 95% CI 1.29-23.30, $p=0.022$).

Association between lung score and study endpoints

The lung score was associated with the endpoints of the need for advanced ventilatory support, anti-COVID medication use, myocardial injury, hospital length of stay, mechanical ventilation, ADHF, in-hospital death, and with the composite endpoint (unadjusted OR 1.44, 95% CI 1.18-1.77).

Multivariate analysis adjusting for the above pertinent variables revealed that the continuous lung score was independently associated with a higher probability for the composite endpoint (OR 1.56; 95% CI 1.12-2.03, $p=0.001$).

Discussion

The current study is, to the best of our knowledge, the first to investigate the utility of hand-held echocardiogram in COVID-19 hospitalized patients to predict endpoints based on identified cardiac abnormalities. COVID-19 hospitalized patients with an abnormal echocardiogram presented with a higher proportion of comorbidities and worse baseline functioning. Abnormal ventricular function/size or significant valvular pathology identified using hand-held ultrasound are associated with worse endpoints

and are independently predictive of the composite endpoint of death, mechanical ventilation, shock and ADHF. Also, the lung score using a hand-held ultrasound is associated with worse endpoints and is independently predictive of the composite endpoint. Among low-risk patients with room-air oxygen saturation $\geq 94\%$ the prevalence of the composite endpoint is very low (3.1%) and focused echocardiogram has a positive predictive value of only 14.3% in this group of patients.

COVID-19 is known to manifest a wide spectrum of cardiac pathologies and the utilization of echocardiogram in these patients has an important role in the settings of myocarditis, acute coronary syndrome, cardiomyopathy, pericardial effusion, arrhythmia and shock. Thus, a timely echocardiogram is integral to the clinical evaluation and management of COVID-19 patients. The burden of the pandemic on healthcare systems necessitates achieving an appropriate balance between the relative necessity of the exam and the duty of sonographers, nurses, advanced practice providers, and physicians to provide high-quality imaging while limiting viral spread, reducing staff exposure and protecting patients. In these settings, traditional criteria for echocardiogram use seem too extensive and clinicians are required to prioritize the need for this valuable resource. The handheld devices have smaller non-sterile exposed areas compared to standard machines, can be easily decontaminated with disinfectant wipes and their size allows for them to be entirely enclosed by a sterile covering thereby limiting iatrogenic virus transmission.[12,13] The findings of the current study support the acquisition of a cardiac assessment sonographic tool that can be dedicated to the COVID-19 departments and can be operated more conveniently in accordance with recommended precautions.

An abnormal echocardiogram was observed in 25.5% of the study population. Other studies using standard cart-based machines or laptops and conducted on COVID-19

hospitalized patients have found a relatively high rate of sonography-based cardiac abnormalities ranging up to 68% with RV systolic dysfunction being the most predominant finding (10-52.8%).[14-20] This discrepancy may be explained by selection bias (patients with advanced illness), differing timelines between echocardiogram performance and disease onset, lack of Doppler usage, partial RV visualization, and discrepancies in the definition of an abnormal echocardiogram. Another important difference is the use of high-end devices or detailed full echocardiogram examinations in most of the studies. As none of the studies used hand-held ultrasound, their examination may be more meticulous but less practical in the COVID-19 clinical setting.

An example of studies focusing on patients with advanced illness is one in which an echocardiogram was only performed after approval by three physicians and on patients with an elevated high sensitivity troponin or a clinical need for the exam. [19] In this study, 82% of the patients required mechanical ventilation and 58% required vasopressor support. A correlation between disease severity and the prevalence of an abnormal echocardiogram can be found in a cross-sectional study comparing patients with non-severe COVID-19 to those with severe disease, demonstrating larger biventricular diameters alongside lower LVEF and RV FAC in those with severe disease.[21]

An association between mortality and cardiac abnormality on echocardiogram was also found in Karagodin et al., demonstrating an association between both LV and RV strain and mortality.[22] However, the routine utilization of strain for ventricular assessment is limited for patients hospitalized in COVID-19 designated departments. Also, unlike in our study, their cohort included a very high in-hospital mortality rate of 21.6% that may reflect selection bias of patients with more severe COVID-19.

Limitations

This is a prospective, single-center, observational study and not a randomized trial, and as such is subjected to associated confounding factors. However, after constructing a multivariate analysis, the independent predictive value remained substantial. Also, data regarding prior echocardiogram studies are lacking and not included in the analysis. Lack of pulsed and continuous-wave Doppler usage and simultaneous electrocardiogram limit the evaluation of valvular pathologies, hemodynamics, and echocardiographic images which may have led to an underestimation of cardiac pathologies. Nonetheless, the study provides data in real-world settings that are relevant to the day-to-day limited clinical use of POCUS echocardiogram in COVID-19 wards. A prospective POCUS study with non-cardiologists vs. cardiologists and low-risk vs. high-risk patients would assist in clarifying the limitations of the current study.

Conclusion

Abnormal echocardiogram results in hospitalized COVID-19 patients when performed by a cardiologist or intensivist and interpreted by a fellowship-trained echocardiographer in a tertiary care setting are associated with a higher burden of comorbidities and independently predict major adverse endpoints. Hand-held POCUS of hospitalized COVID-19 patients can be utilized as an important “rule-out” tool among high-risk patients with room-air oxygen saturation $<94\%$ and should be integrated as part of their routine admission evaluation. The routine utilization of focused echocardiogram among low-risk patients is not recommended for prognostication or as a screening tool.

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References

1. Zhou F, Ting Yu, Ronghui Du, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020; 395: 1054-62. doi: 10.1016/S0140-6736(20)30566-3.
2. <https://www.escardio.org/Education/COVID-19-and-Cardiology/ESC-COVID-19-Guidance>. Accessed September 22, 2021.
3. Kirkpatrick JN, Mitchell C, Taub C, et al. ASE Statement on Protection of Patients and Echocardiography Service Providers During the 2019 Novel Coronavirus Outbreak: Endorsed by the American College of Cardiology. *J Am Soc Echocardiogr*. 2020; 33: 648-653. doi: 10.1016/j.echo.2020.04.001.
4. Skulstad H, Cosyns B, Popescu BA, et al. COVID-19 pandemic and cardiac imaging: EACVI recommendations on precautions, indications, prioritization, and protection for patients and healthcare personnel. *Eur Heart J Cardiovasc Imaging*. 2020; 21: 592-598. doi: 10.1093/ehjci/jeaa072.
5. Stoica R, Heller EN, Bella JN. Point-of-care screening for left ventricular hypertrophy and concentric geometry using hand-held cardiac ultrasound in hypertensive patients. *Am J Cardiovasc Dis*. 2011; 1: 119-25.
6. Khan HA, Wineinger NE, Uddin PQ, Mehta HS, Rubenson DS, Topol EJ. Can hospital rounds with pocket ultrasound by cardiologists reduce standard echocardiography? *Am J Med*. 2014; 127: 669.e1-7. doi: 10.1016/j.amjmed.2014.03.015.
7. Moore CL, Copel JA. Point-of-care ultrasonography. *N Engl J Med*. 2011; 364: 749-57. doi: 10.1056/NEJMr0909487.

8. Dietrich CF, Goudie A, Chiorean L, et al. Point of care ultrasound: a WFUMB position paper. *Ultrasound Med Biol*. 2017; 43: 49-58. doi: 10.1016/j.ultrasmedbio.2016.06.021.
9. McKaigney CJ, Krantz MJ, La-Rocque CL, Hurst ND, Buchanan MS, Kendall JL. E-point septal separation: a bedside tool for emergency physician assessment of left ventricular ejection fraction. *Am J Emerg Med*. 2014; 32: 493-7. doi: 10.1016/j.ajem.2014.01.045.
10. Wright J, Jarman R, Connolly J, Dissmann P. Echocardiography in the emergency department. *Emerg Med J*. 2009; 26: 82-6. doi: 10.1136/emj.2008.058560.
11. Kiamanesh O, Harper L, Wiskar K, et al. Lung Ultrasound for Cardiologists in the Time of COVID-19. *Can J Cardiol*. 2020; 36: 1144-7. doi: 10.1016/j.cjca.2020.05.008.
12. Jenkins S, Garg P. Prime time for handheld echocardiography in COVID-19 pandemic. *Clin Med (Lond)*. 2020; 20: e132. doi: 10.7861/clinmed.Let.20.4.3.
13. Gibson LE, Bittner EA, Chang MG. Handheld ultrasound devices: An emerging technology to reduce viral spread during the Covid-19 pandemic. *Am J Infect Control*. 2020; 48: 968-969. doi: 10.1016/j.ajic.2020.05.041.
14. Szekely Y, Lichter Y, Taieb P, et al. Spectrum of cardiac manifestations in COVID-19: a systematic echocardiographic study. *Circulation*. 2020; 142: 342-353. doi: 10.1161/CIRCULATIONAHA.120.047971.
15. Li Y, Li H, Li M, Zhang L, Xie M. The prevalence, risk factors and outcome of cardiac dysfunction in hospitalized patients with COVID-19. *Intensive Care Med*. 2020; 46: 2096-2098. doi: 10.1007/s00134-020-06205-0.

16. Jain SS, Liu Q, Raikhelkar J, et al. Indications for and findings on transthoracic echocardiography in COVID-19. *J Am Soc Echocardiogr.* 2020; 33: 1278-1284. doi: 10.1016/j.echo.2020.06.009.
17. Moody WE, Mahmoud-Elsayed HM, Senior J, et al. Impact of right ventricular dysfunction on mortality in patients hospitalized with COVID-19, according to race. *CJC open.* 2021; 3: 91-100. doi: 10.1016/j.cjco.2020.09.016.
18. Van den Heuvel FM, Vos JL, Koop Y, et al. Cardiac function in relation to myocardial injury in hospitalised patients with COVID-19. *Neth Heart J.* 2020; 28: 410-417. doi: 10.1007/s12471-020-01458-2.
19. Mahmoud-Elsayed HM, Moody WE, Bradlow WM, et al. Echocardiographic findings in patients with COVID-19 pneumonia. *Can J Cardiol.* 2020; 36: 1203-1207. doi: 10.1016/j.cjca.2020.05.030.
20. Dweck MR, Bularga A, Hahn RT, et al. Global evaluation of echocardiography in patients with COVID-19. *Eur Heart J Cardiovasc Imaging.* 2020; 21: 949-958. doi: 10.1093/ehjci/jeaa178.
21. Barman HA, Atici A, Tekin EA, et al. Echocardiographic features of patients with COVID-19 infection: a cross-sectional study. *Int J Cardiovasc Imaging.* 2021; 37: 825-834. doi: 10.1007/s10554-020-02051-9.
22. Karagodin I, Singulane CC, Woodward GM, et al. Echocardiographic Correlates of In-Hospital Death in Patients with Acute COVID-19 Infection: The World Alliance Societies of Echocardiography (WASE-COVID) Study. *J Am Soc Echocardiogr.* 2021; 21: S0894-731700483-1. doi: 10.1016/j.echo.2021.05.010.

Table 1. Baseline and clinical characteristics.

Variable	All	Normal	Abnormal	<i>p</i> -value
	n=102	echocardiogram n=76	echocardiogram n=26	
Baseline characteristics				
Age, mean ± SD	59.7 ± 18.4	57.0 ± 18.6	67.6 ± 15.5	0.010
Male, n (%)	65 (63.7)	48 (63.2)	17 (65.4)	0.838
Body mass index, mean ± SD	27.9 ±6.2	27.6 ±6.2	28.9 ±6.2	0.378
Smoking, n (%)	16 (15.7)	8 (10.5)	8 (30.8)	0.014
Diabetes mellitus, n (%)	33 (32.4)	21 (27.6)	12 (46.2)	0.081
Hypertension, n (%)	39 (38.2)	23 (30.3)	16 (61.5)	0.005
Hyperlipidemia, n(%)	32 (31.4)	18 (23.7)	14 (53.8)	0.004
IHD, n (%)	20 (19.6)	9 (11.8)	11 (42.3)	0.001
CVA, n (%)	5 (4.9)	2 (2.6)	3 (11.5)	0.103
Revascularization, n (%)	17 (16.7)	7 (9.2)	10 (38.5)	0.001
Heart failure, n (%)	12 (11.8)	3 (3.9)	9 (34.6)	<0.001
Valve replacement, n (%)	3 (2.9)	0 (0.0)	3 (11.5)	0.015
CIED, n (%)	3 (2.9)	0 (0.0)	3 (11.5)	0.015
Cognitive decline, n (%)	23 (22.5)	14 (18.4)	9 (34.6)	0.088
Debilitation, n (%)	26 (25.5)	16 (21.1)	10 (38.5)	0.079
Chronic lung disease, n (%)	9 (8.8)	6 (7.9)	3 (11.5)	0.690
Liver disease, n (%)	2 (2.0)	2 (2.6)	0 (0.0)	1.000
Prior VTE, n (%)	4 (3.9)	2 (2.6)	2 (7.7)	0.268

Malignancy, n (%)	2 (2.0)	1 (1.3)	1 (3.8)	0.447
Immunosuppression, n (%)	4 (3.9)	3 (3.9)	1 (3.8)	1.000
Hypothyroidism, n (%)	13 (12.7)	8 (10.5)	5 (19.2)	0.251
Chronic medications				
ACE-I/ARB, n (%)	24 (23.5)	14 (18.4)	10 (38.5)	0.038
β-blockers, n (%)	29 (28.4)	15 (19.7)	14 (53.8)	0.001
CCB, n (%)	12 (11.8)	9 (11.8)	3 (11.5)	1.000
Anti-platelets, n (%)	26 (25.5)	12 (15.8)	14 (53.8)	<0.001
Oral anticoagulation, n (%)	13 (12.7)	8 (10.5)	5 (19.2)	0.251
Diuretics, n (%)	11 (10.8)	4 (5.3)	7 (26.9)	0.005
Inhalations, n (%)	7 (6.9)	5 (6.6)	2 (7.7)	1.000
SGLT2 inhibitors, n (%)	7 (6.9)	5 (6.6)	2 (7.7)	1.000
Statins, n (%)	33 (32.4)	17 (22.4)	16 (61.5)	<0.001
COVID-19 presentation				
Chest pain, n (%)	28 (27.5)	22 (28.9)	6 (23.1)	0.563
Shortness of breath, n (%)	54 (52.9)	37 (48.7)	17 (65.4)	0.141
HR (bpm) , mean ± SD	88.8 ± 22.3	88.1 ± 19.3	90.7 ± 30.0	0.626
SBP (mmHg), mean ± SD	124.3 ± 20.9	123.4 ± 19.9	126.8 ± 23.7	0.461
DBP (mmHg), mean ± SD	74.1 ± 12.0	73.6 ± 11.2	75.6 ± 14.3	0.375
SpO2 (%), mean ± SD	87.4 ± 11.4	87.3 ± 11.9	87.8 ± 10.3	0.752
In-hospital course				
Sinus bradycardia, n (%)	2 (2.0)	2 (2.7)	0 (0.0)	1.000
ECG changes				0.040
Normal, n (%)	74 (72.5)	59 (77.6)	15 (57.7)	
Nonspecific changes, n (%)	19 (18.6)	12 (15.8)	7 (26.9)	

TWI/ ST-depression, n (%)	6 (5.9)	4 (5.3)	2 (7.7)	
ST-elevation, n (%)	2 (2.0)	0 (0.0)	2 (7.7)	
Chest X-ray infiltrates, n (%)	75 (73.5)	51 (67.1)	24 (92.3)	0.012
AF/AFL, n (%)	11 (10.8)	7 (9.2)	4 (15.4)	0.130

Lab results

WBC (p), mean \pm SD	10.4 \pm 5.7	9.6 \pm 5.0	12.8 \pm 6.7	0.013
ANC/ALC (a), median (IQR)	5.9 (3.0-10.6)	5.4 (2.6-8.9)	9.0 (4.4-13.4)	0.032
Hemoglobin (a), mean \pm SD	13.0 \pm 2.3	13.1 \pm 2.1	12.6 \pm 2.7	0.240
Platelets (a), mean \pm SD	200.6 \pm 73.6	203.0 \pm 73.3	193.2 \pm 75.3	0.802
Creatinine (a), mean \pm SD	1.0 \pm 0.7	0.9 \pm 0.4	1.4 \pm 1.1	0.002
K (a), mean \pm SD	4.0 \pm 0.6	3.9 \pm 0.5	4.1 \pm 0.7	0.168
Albumin (t), mean \pm SD	3.0 \pm 0.8	3.1 \pm 0.8	2.6 \pm 0.7	0.044
Hs-cTnI (p), median (IQR)	7.0 (5.0-40.8)	5.5 (5.0-22.0)	37 (6.5-541.5)	0.001
BNP (a), median (IQR)	76.5 (22.5-229.5)	59.8 (15.0-200.8)	224.5 (94.5-753.5)	0.065
CRP (p), mean \pm SD	13.0 \pm 11.8	11.2 \pm 11.6	18.2 \pm 10.9	0.003
D-dimer (p), median (IQR)	925 (522-1188)	803 (392-1362)	1178 (878-2707)	0.014
Fibrinogen (a), mean \pm SD	594.9 \pm 186.5	572.9 \pm 187.8	660.1 \pm 169.3	0.015
aPTT (p), mean \pm SD	35.0 \pm 9.7	33.9 \pm 9.7	38.1 \pm 9.2	0.009

Abbreviations a, admission; ACE-I, angiotensin-converting enzyme; AF, atrial fibrillation; AFL, atrial flutter; ALC, absolute lymphocytes count; ANC, absolute neutrophils count; aPTT, activated partial thromboplastin time; ARB, angiotensin receptor blocker; BNP, brain natriuretic peptide; bpm, beats per minute; CCB, calcium channel blocker; CIED, cardiovascular implantable electronic device; CRP, c-reactive protein; CVA, cerebrovascular accident; DBP, diastolic blood pressure; ECG, electrocardiogram; HR, heart rate; Hs-cTnI, high sensitive cardiac troponin I; IHD, ischemic heart disease; IQR,

interquartile range; K, potassium; mmHg, millimeter of mercury; n, number; p, peak; SD, standard deviation; SBP, systolic blood pressure; SGLT2, sodium-glucose transport protein 2; SpO₂, oxygen saturation; t, trough; TWI, T-wave inversion; VTE, venous thromboembolism; WBC, white blood cells.

Table 2. Echocardiography results, measurements, and lung ultrasound score for patients with and without in-hospital advanced ventilatory support.

Parameter	All n=102	Normal echocardiogram n=76	Abnormal echocardiogram* n=26	p-value [†]	No advanced ventilatory support n=76	Advanced ventilatory support n=26	p-value ⁺
LVEF (%), mean \pm SD	53.4 \pm 6.8	57.2 \pm 4.1	49.2 \pm 8.2	<0.001	55.8 \pm 6.3	53.4 \pm 6.6	0.096
LVEF <50%, n (%)	16 (15.7)	0 (0.0)	16 (61.5)	<0.001	9 (11.8)	7 (26.9)	0.068
LVEDD (cm), mean \pm SD	4.6 \pm 0.5	4.5 \pm 0.5	4.8 \pm 0.6	0.016	4.6 \pm 0.6	4.6 \pm 0.5	0.692
RV dysfunction, n (%)	8 (7.8)	0 (0.0)	8 (30.8)	<0.001	5 (6.6)	3 (11.5)	0.425
RV dilation, n (%)	7 (6.7)	0 (0.0)	7 (26.9)	<0.001	5 (6.6)	2 (7.7)	1.000
Ventricular abnormality, n (%)	24 (23.5)	0 (0.0)	24 (92.3)	<0.001	14 (18.4)	10 (38.5)	0.034
TAPSE (cm), mean \pm SD	1.9 \pm 0.3	2.0 \pm 0.3	1.8 \pm 0.2	0.159	2.0 \pm 0.3	1.8 \pm 0.2	0.045
FAC (%), mean \pm SD	35.2 \pm 6.5	35.6 \pm 6.0	34.1 \pm 7.7	0.518	34.9 \pm 6.5	36.4 \pm 6.7	0.563
Significant MR, n (%)	7 (6.9)	0 (0.0)	7 (26.9)	<0.001	4 (5.3)	3 (11.5)	0.365
Significant TR, n (%)	6 (5.9)	0 (0.0)	6 (23.1)	<0.001	3 (3.9)	3 (11.5)	0.167

Significant AS, n (%)	6 (5.9)	0 (0.0)	6 (23.1)	<0.001	4 (5.3)	2 (7.7)	0.636
Significant valvulopathy, n (%)	9 (8.8)	0 (0.0)	9 (34.6)	<0.001	5 (6.6)	4 (15.4)	0.225
Pericardial effusion, n (%)	6 (5.9)	0 (0.0)	6 (23.1)	<0.001	3 (3.9)	3 (11.5)	0.171
Lung score, mean \pm SD	3.1 \pm 2.4	2.9 \pm 2.4	3.7 \pm 2.5	0.119	2.7 \pm 2.3	4.5 \pm 2.4	0.001

[‡] P-value was calculated for the difference of normal echocardiogram to abnormal.

⁺ P-value was calculated for the difference of advanced ventilatory support to no support.

* Abnormal echocardiogram was defined as left or right ventricular dysfunction or enlargement, or moderate/severe valvular regurgitation/stenosis echocardiographic study.

Abbreviations. AS, aortic stenosis; FAC, fractional area change; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; n, number; RV, right ventricle; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

Table 3. The association between abnormal echocardiogram and serious adverse events (endpoints).

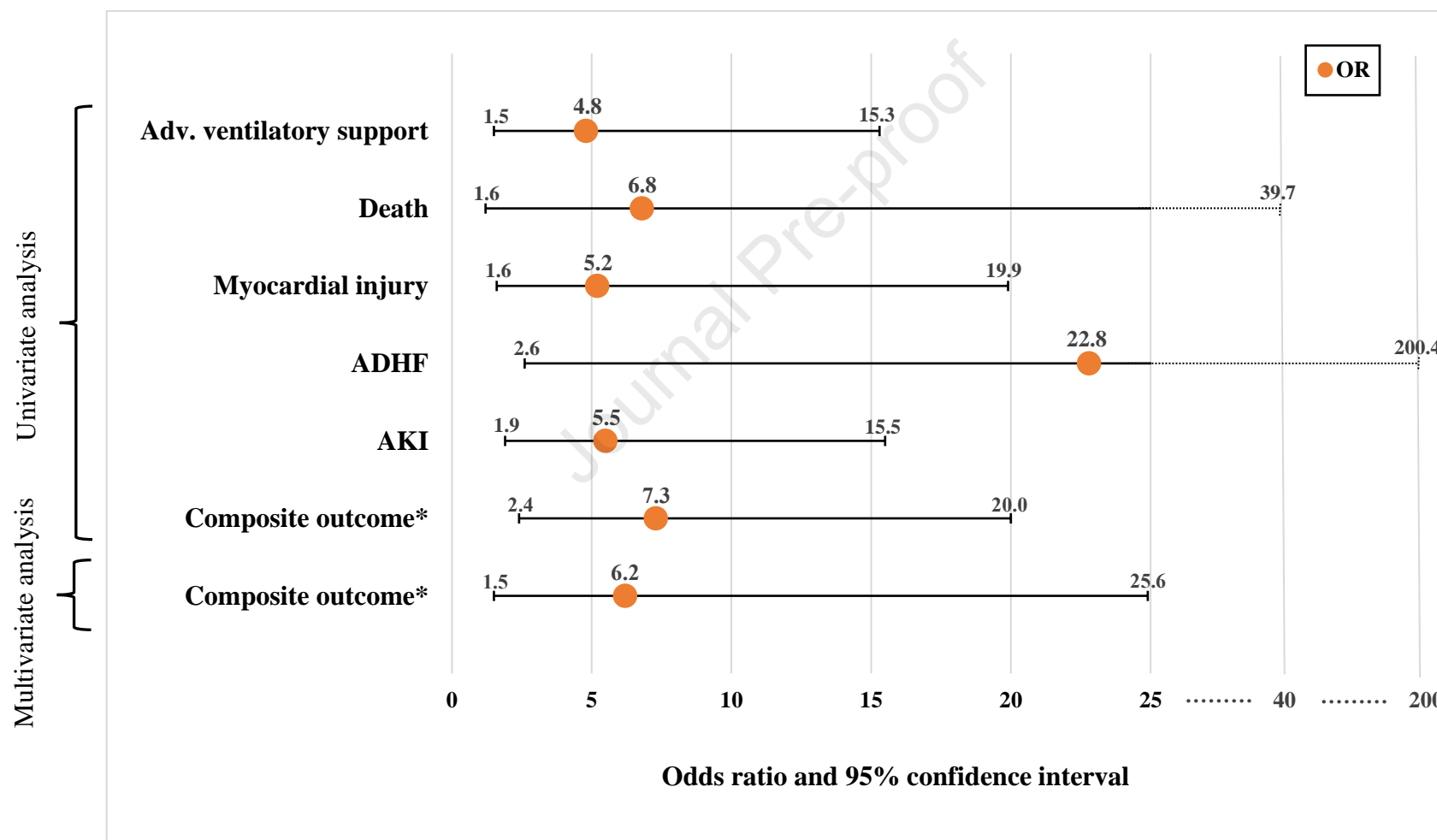
Variable	All n=102	Normal echocardiography n=76	Abnormal echocardiography n=26	p-value	Unadjusted OR (95% CI)
Composite outcome*, n (%)	20 (19.6)	8 (10.5)	12 (46.2)	<0.001	7.29 (2.44-20.00)
In-hospital death, n (%)	6 (5.9)	2 (2.6)	4 (15.4)	0.033	6.82 (1.2-39.7)
Mechanical ventilation, n (%)	12 (11.8)	7 (9.2)	5 (19.2)	0.164	2.38 (0.68-8.29)
Shock, n (%)	7 (6.9)	4 (5.3)	3 (11.5)	0.249	2.35 (0.5-11.3)
ADHF, n (%)	6 (5.9)	0 (0.0)	6 (23.1)	0.005	22.8 (2.6-200.4)
Advanced ventilatory support, n (%)	26 (25.5)	15 (19.7)	11 (42.3)	0.021	4.83 (1.5-15.3)
Myocardial injury, n (%)	14 (13.7)	6 (7.9)	8 (30.8)	0.003	5.19 (1.6-19.9)
Chronic ventilation, n (%)	9 (8.8)	6 (7.9)	3 (11.5)	0.414	1.52 (0.4-6.6)
Venous thromboembolism, n (%)	3 (2.9)	2 (2.6)	1 (3.8)	1.000	1.48 (0.1-17.0)
Anti-COVID drugs, n (%)	40 (39.2)	27 (35.5)	13 (50.0)	0.192	1.82 (0.7-4.7)
Sepsis, n (%)	11 (10.8)	6 (7.9)	5 (19.2)	0.108	2.78 (0.8-10.0)

Acute kidney injury, n (%)	20 (19.6)	9 (11.8)	11 (42.3)	0.001	5.46 (1.9-15.5)
New renal replacement therapy, n (%)	3 (2.9)	0 (0.0)	3 (11.5)	0.052	9.9 (0.98-99.9)
LOS (days), median [IQR]	8.1 [3.0,16.3)	7 [2.8,14.1]	10.4 [6.8,29.3]	0.202	5.07 (-2.75-12.89)

* Composite outcome included: in-hospital death, mechanical ventilation, shock and acute decompensated heart failure.

Abbreviations ADHF, acute decompensated heart failure; CI, confidence interval; IQR, interquartile range; LOS, length of stay; n, number; OR, odds ratio.

Figure 1. Significant associations (odds ratio and 95% confidence interval⁺) between abnormal echocardiogram and serious adverse events (endpoints)

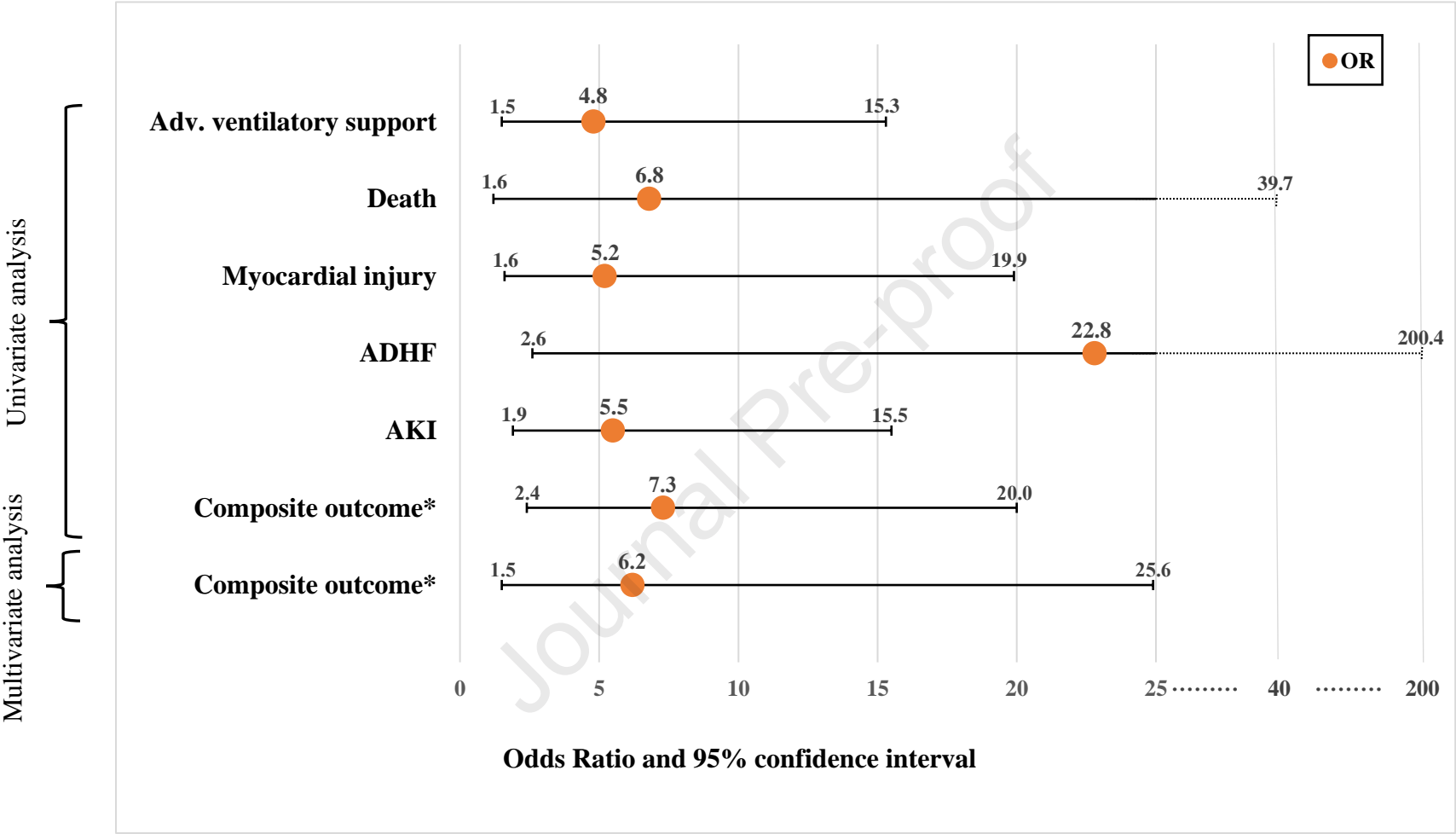


* The primary endpoint was defined as a composite endpoint of in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure.

⁺ Numeric results of OR and 95% CI and are detailed in *Table 3*.

Abbreviations ADHF, acute decompensated heart failure; Adv., advanced; AKI, acute kidney injury; OR, odds ratio.

Figure 1. Significant associations (odds ratio and 95% confidence interval⁺) between abnormal echocardiogram and serious adverse events (endpoints)



* The primary endpoint was defined as a composite endpoint of in-hospital death, mechanical ventilation, shock, and acute decompensated heart failure.

+ Numeric results of OR and 95% CI and are detailed in Table 3.

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